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Dear Dr. Thayer:

On behalf of the Soy Nutrition Institute (SNI), we would like to commend the CERHR Expert Panel for their thorough evaluation and review of the literature related to soy infant formula. We acknowledge and respect the panel's conclusion; however, based on the data presented in the report, our view is that there was inadequate justification to raise the level of concern for adverse developmental effects from "negligible" to "minimal." Furthermore, the report did not adequately indicate why the concern level was changed. It would be helpful for investigators to understand the primary basis upon which the expert panel raised the concern level. Doing so would allow researchers to conduct appropriately designed studies evaluating soy infant formula.

The panel does allude to the reason for elevating the level of concern in the fourth bullet in the Overall Conclusions. Namely, "… a number of studies in experimental animals and one study in humans reported effects related to the reproductive system and this elevates the concern from "negligible" to "minimal." It is difficult, without further explanation, to understand how this small number of studies, only one of which involved humans, carried sufficient weight to influence the panel's overall conclusions. The one human study, which was rated as having limited utility, is a small epidemiologic investigation published 25 years ago that found soy infant formula use was associated with an increased risk of premature thelarche (1). However, the findings of this study have been challenged on several grounds (2, 3). Furthermore, there has not been one published case report of premature thelarche being attributed to soy infant formula use among the millions of American infants that have used this product over the past 40 years.

In section 4.5 "Critical Data Gaps and Research Needs," several suggestions are made for additional research to better understand the effects of soy infant formula on reproductive and non-reproductive endpoints. We concur with the panel that there are gaps in the pharmacokinetic data on isoflavones. However, isoflavones are not unique in that there are many biological active components in cow's milk formula for which pharmacokinetic data do not exist.

We concur with the points raised concerning animal experimentation (section 4.5.3). The panel points out the limitations of using rodents in general as models for human exposure.

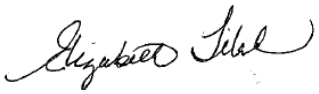
In addition, most studies to date have not used intact soy infant formula but only isolated components. Since there are interactions among biologically active components of foods that potentially impact the health effects of a food, it does not seem fruitful to continue to pursue studies using isolated components from soybeans as a means of evaluating the biologic activity of the formula (4). Furthermore, as concluded by the panel: "The relevance of some developmental effects to human health, such as vaginal opening (time of puberty onset) in rodents, is uncertain." Since animal studies cannot provide compelling evidence for potential effects of soy infant formula in humans, the value of continuing to rely on these models for substantive information is questionable.

This point warrants particular emphasis because the Beginnings Study, which is currently underway at the University of Arkansas, holds the potential to provide extremely meaningful data within the next couple of years (5). In this study, a wide range of hormone-related developmental endpoints are being examined in infants fed breast milk, soy infant formula or cow's milk formula. The panel appropriately cited cross contamination (some infants in each group were exposed to more than one type of feeding regimen) and the small number of infants for which data were available as limitations of this study. However, by study completion there will be large numbers of infants in each group who will have been fed only one way from birth.

In conclusion, soy infant formula remains a healthful and important option for mothers and pediatricians who, for a variety of reasons, cannot or choose not to breast feed or use cow's milk formula. The American Academy of Pediatrics Committee on Nutrition (AAP-CON) (6) has concluded that "soy protein-based formulas may be used to provide nutrition for normal growth and development". The AAP-CON (6) and the European Society of Paediatric Gastroenterology, Hepatology, and Nutrition (7) agree that soy-based infant formulas are safe and effective for use in infants with severe persistent lactose intolerance including primary (hereditary) lactase deficiency and classic galactosemia. The AAP also recognizes that soy infant formula can be used successfully in cases of secondary lactase deficiency and when a vegetarian diet is preferred. Further, a 2008 Australian consensus panel recommends soy-based infant formula for the management of IgE-mediated cow milk allergy (8), a recommendation that is supported by subsequently published research (9). Clearly, soy infant formula is a necessary, safe, nutritious and effective choice for parents and pediatricians dealing with a variety of feeding issues and circumstances.

We encourage the Expert Panel to exercise caution when communicating their final summary and conclusion of the CERHR report to make it clear what "minimal" level of concern actually means in practice to parents and pediatricians choosing soy infant formula. It is important not to alarm parents who have currently chosen soy infant formula or to unjustifiably dissuade parents from doing so in the future.

Sincerely,



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References

1. Freni-Titulaer LW, Cordero JF, Haddock L, Lebron G, Martinez R, Mills JL. Premature thelarche in Puerto Rico. A search for environmental factors. Am J Dis Child. 1986;140:1263-7.
2. Anonymous. Precocious development in Puerto Rican children. Lancet. 1986;1:721-2.
3. Hannon WH, Hill RH, Jr., Bernert JT, Jr., Haddock L, Lebron G, Cordero JF. Premature thelarche in Puerto Rico: a search for environmental estrogenic contamination. Arch Environ Contam Toxicol. 1987;16:255-62.
4. Messina M, Lampe JW, Birt DF, Appel LJ, Pivonka E, Berry B, Jacobs DR, Jr. Reductionism and the narrowing nutrition perspective: time for reevaluation and emphasis on food synergy. J Am Diet Assoc. 2001;101:1416-9.
5. Gilchrist JM, Moore MB, Andres A, Estroff JA, Badger TM. Ultrasonographic patterns of reproductive organs in infants fed soy formula: comparisons to infants fed breast milk and milk formula. J Pediatr.156:215-20.
6. Bhatia J, Greer F. Use of soy protein-based formulas in infant feeding. Pediatrics. 2008;121:1062-8.
7. Agostoni C, Axelsson I, Goulet O, Koletzko B, Michaelsen KF, Puntis J, Rieu D, Rigo J, Shamir R, et al. Soy Protein Infant Formulae and Follow-On Formulae: A Commentary by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2006;42:352-61.
8. Kemp AS, Hill DJ, Allen KJ, Anderson K, Davidson GP, Day AS, Heine RG, Peake JE, Prescott SL, et al. Guidelines for the use of infant formulas to treat cows milk protein allergy: an Australian consensus panel opinion. Med J Aust. 2008;188:109-12.
9. Sladkevicius E, Nagy E, Lack G, Guest JF. Resource implications and budget impact of managing cow milk allergy in the UK. J Med Econ. 2010;13:119-28.